

REMARKS

Applicant has considered the non-final office action mailed June 22, 2010 in connection with the Application.

Reference herein to pages and line numbers of the specification of the Application are with respect to the specification of international application no. PCT/GB04/05030, of which the Application is the U.S. national phase.

Amendments to the Claims

Claims 1 – 26 are pending in the Application prior to entry of the Amendments herein. In the instant section, it is to be assumed that reference herein to a single portion of the specification in support of a particular amendment or new claim, is not to preclude the existence of additional support for that amendment or claim, but located elsewhere in the specification and drawings, and not specifically referenced herein.

Claims 1 and 2 are cancelled herein without prejudice to Applicant's rights to pursue the subject matter of the claims in one or more continuing applications that benefit of the right of priority of the Application.

Claim 3 is amended to exclude various substituents, and to attend to a misplaced item of punctuation. Support for such an exclusion can be found in Applicant's specification at, for example, pages 9 – 10.

Claim 4 is amended to attend to an item of grammar, and to provide a definition of substituent 'X'. Support for such an exclusion can be found in Applicant's specification at, for example, pages 9 – 10.

Claim 5 is amended to exclude various substituents, and to attend to a misplaced item of punctuation.

Claim 6 is amended to attend to various items of grammar.

Claims 8 – 14 are amended to correct their respective dependencies and/or preambles.

Claim 15 is amended to attend to an informality of grammar.

Claims 16 and 18 are amended to delete one or more of the listed compounds, and to attend to an informality of grammar.

An Applicant may decline to claim any material disclosed in his specification. MPEP 2173.05(i); *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187,196 (CCPA 1977) (alternative elements positively recited in the specification may be explicitly excluded in the claims).

Claims 19 – 23 are amended to correct their respective dependencies, preambles and/or items of antecedent basis.

Claim 25 is amended to attend to an informality of grammar.

New claims 27 – 29 are supported by the original disclosure and or originally-filed claims.

Accordingly, no new matter is introduced by way of the new claims herein and entry thereof is respectfully requested.

REJECTIONS OF THE CLAIMS

Rejections under 35 U.S.C. § 101

The Examiner has rejected claims 1, 2, 7 – 14, 19, and 21 – 23 under 35 U.S.C. § 101 as allegedly being drawn to non-statutory subject matter, specifically because the claims recite a “use, without setting forth any steps involved in the process.”

Applicant has cancelled claims 1 and 2 herewith, thereby mooting the rejection of those claims.

The preambles to claims 7 – 14, 19, and 21 – 23 have been amended to recite different statutory classes, thereby also overcoming the rejection.

Accordingly, Applicant requests that the Examiner withdraw the rejection of claims under 35 U.S.C. § 101.

Rejections under 35 U.S.C. § 112 (¶ 2)

The Examiner has rejected claims 1, 2, 7 – 14, 19, and 21 – 23 under 35 U.S.C. § 112 (second paragraph) as allegedly being indefinite for “merely reciting a use without any active, positive steps delimiting how the use is actually practiced”.

The rejection under the second paragraph of 35 U.S.C. § 112 mirrors the rejection under 35 U.S.C. § 101, which has been addressed by cancelling claims 1 and 2, and amending the preambles of the other claims.

Accordingly, the rejection of claims under 35 U.S.C. § 112 (second paragraph) should also be withdrawn.

Rejections under 35 U.S.C. § 112 (¶ 1)

Scope of Enablement

The Examiner has rejected claims 1 – 26 under 35 U.S.C. § 112 (first paragraph) as allegedly being based on a disclosure that is not enabled commensurate in scope with the claims. Applicant respectfully traverses the rejection.

First, Applicant respectfully submits that the Examiner's rejection appears to be based upon a misapprehension of Applicant's disclosure. The Examiner's rejection is framed as follows:

[T]he specification, while being enabling for using the compound of formula I, wherein compounds claimed in claims 15, 16, 17, 18, 21, 22, 23, 24, 25, and 26 are synthesized from general formula I does not reasonably provide enablement for making the same.

(June 22, 2010 Office Action at page 3; emphasis herein). Furthermore, the Examiner states that “[t]he instant claims requires [*sic*] synthesizing compound formula I to produce the compounds I” (June 22, 2010 Office Action at page 4).

This interpretation is incorrect. Nowhere does Applicant's disclosure suggest that compounds of formula I' are synthesized from compounds of formula I. In fact, as described in Applicant's disclosure, at for example pages 4, 5, and 8, the compounds of formula I' are simply one of two possible enantiomeric forms of the compounds of formula I (due to the asymmetry at the carbon atom at the 3-position in the ring).

Nevertheless, Applicant addresses what is possibly the underlying concern of the Examiner, that there is a lack of synthetic data in Applicant's disclosure, as follows.

Based on the Examiner's interpretation that there is a lack of synthetic data to derive specific compounds from those of “general formula I”, the Examiner then applies the *Wands* factors to the claims. In particular, the Examiner states that the

[d]isclosure lacks a clear teaching, direction of guidance as to how to prepare compounds of the instantly claimed general formula. There are none [*sic*] specific teaching to the synthesis of the particular compound under examination and none [*sic*] specific schema in the instant disclosure to provide a method of synthesizing a compound of the structure presently under examination.

(June 22, 2010 Office Action at pages 4 – 5). The Examiner also states that:

“absent any direction or guidance as to how the skilled artisan would go about synthesizing the claimed compound ... one of ordinary skill in the

art would have ... to undertake an exhaustive and, thus, unduly burdensome, search for ways to synthesize this embodiment”.

(June 22, 2010 Office Action at page 6). The Examiner states further that:

“Applicant has (1) failed to provide any clear general synthetic procedures to the instantly claimed compound of the general formula or (2) failed to provide any working or prophetic examples directed to a possible method and/or manner of synthesis for the instantly claimed compound of the general formula.”

(June 22, 2010 Office Action at pages 6 – 7). Again, Applicant respectfully disagrees.

Applicant believes that the Examiner has overlooked a considerable volume of Applicant’s disclosure, that is directed to general methods of synthesis of compounds of formulae I and I’, as well as to examples of synthesis of specific compounds.

Applicant draws the Examiner’s attention to the Schema on Page 13 of the Application, wherein four (4) synthetic routes to compounds of formula (I) are shown. Description of preferred experimental conditions for those synthetic routes is given on pages 13 – 14 of the Application.

Applicant also points out to the Examiner the Examples shown on pages 16 – 49 of the Application. These examples are all drawn to syntheses of compounds of formula (I) or (I’). Applicant notes that this is not an insignificant number of examples. In fact, synthetic routes to more than sixty (60) compounds of various classes are described, comprising: Forty Eight (48) compounds of formulae (I/I’) (Examples 1 – 34, 40, 41, 42a, 42b, 45, 49, 50a, 50b, 55, 56, 59a, 59b, 61, and 62, on pages 16 – 36, 39 – 40, 42 – 43, 45, 47, and 48 – 49). Furthermore, the synthesis of fourteen (14) Intermediates, useful in synthesis of compounds of the invention, are also described (Examples 35 – 38, 43, 44, 46 – 48, 51 – 54, 57, 58, and 60, on pages 36 – 38, 40 – 42, 43 – 47).

Although the Examiner notes also that, generally, the susceptibility of chemical reactions to variation due to a number of factors, and that, although the “level of skill in the art is high”, and that “experimentation in this particular art is not at all uncommon” the “experimentation required in order to practice this aspect [the synthesis of compounds of formula I] would be *undue*” (June 22, 2010 Office Action at pages 5 – 7; emphasis in original), Applicant believes this reasoning to be mooted by the arguments expressed hereinabove. In particular, given the large number of synthetic examples provided, as well as the several alternative synthetic routes, Applicant’s statements that the synthesis of these compounds would fall within the capability of those of skill

in the art and the Examiner's statement that the level of skill would be high, Applicant believes that the disclosure is fully enabling with respect to methods of synthesis of compounds commensurate in scope with those claimed.

Accordingly, and noting that claims 1 and 2 are cancelled herein, Applicant respectfully requests that the Examiner withdraws the rejection of claims 3 – 26 under 35 U.S.C. § 112 (first paragraph) as not enabled commensurate with their scope.

Enablement

The Examiner has also rejected claim 20 under 35 U.S.C. § 112 (first paragraph) as allegedly being based on a non-enabling disclosure. Applicant respectfully traverses the rejection.

Specifically, the Examiner asserted that “the specification does not reasonably provide enablement for the prophylaxis of the symptoms of an inflammatory disease” as recited in claim 20. With the amendment to claim 20 herein, but without acknowledging the propriety of the rejection and without specifically disclaiming the use of the claimed compounds in prophylaxis, the reference to prophylaxis is deleted.

Accordingly, the rejection of claim 20 is mooted by the amendment herein and Applicant respectfully request that the rejection be withdrawn.

Enablement

The Examiner has rejected claims 1 – 26 under 35 U.S.C. § 112 (first paragraph) as allegedly being based on a non-enabling disclosure. Applicant respectfully traverses the rejection.

Specifically, the Examiner appears to object to the recitation in the claims of “treating inflammatory diseases.” To this end, the Examiner asserts that “[t]he claimed invention does not relate to treating a subject” and that “[v]arious diseases having various different causes are not treatable by a single composition.” (June 22, 2010 Office Action at page 13). The Examiner goes on to provide various reasoning as to why “treatment of an animal broadly” is an underdeveloped art.

Applicant first points out that, although the rejection is applied to claims 1 – 26 (those pending as of the date of the June 22, 2010 Office Action), claims 1 and 2 are cancelled herein, and claims 3 – 18, 21 – 23, 25, 26, and new claims 27 – 29 recite no use limitations. Being drawn to compositions only, Applicant believes that the rejection has been mis-applied, at least with respect to those claims. Accordingly, Applicant addresses the merits of the rejection, as applied to claims 19, 20, and 24.

Regarding the treatment of the symptoms of an inflammatory disease, the specification describes the role played by chemokines (a family of signaling molecules) in inflammatory responses generally (*i.e.*, in a wide variety of diseases). (Application at page 1). The Application further references a class of molecules, termed BSCI's ("Broad Spectrum Chemokine Inhibitors"), that provide a basis for developing new compounds (such as those claimed herein) that may also attack inflammation that arises in a large number of diseases. Accordingly, and appreciating that a single mechanism, or family of closely related mechanisms, is at play in a wide variety of inflammatory disorders, Applicant's specification provides support for the premise that a single compound or class of compounds could have broad application.

Furthermore, the "Pharmacological Study" presented at pages 49 – 55 of the Application establishes that compounds falling within the scope of the claims have anti-inflammatory activity, both *in vitro* and *in vivo*.

Finally, Applicant believes that the Examiner has misunderstood Applicant's claims in at least one respect. Specifically, none of claims 19, 20, or 24, recites a compound that individually is effective against *all* inflammatory disorders. The use of the singular ("an") in claims 20 and 24, and the use of a Markush list in claim 19, means that at least one inflammatory disorder is implicated for a given compound, but does not require all such disorders to fall within the scope of the claim for a given compound.

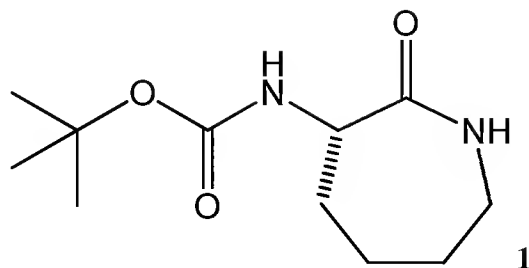
Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. § 112 (first paragraph) of claims 1 – 26, as not enabled, be withdrawn.

Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 1 – 26 under 35 U.S.C. § 102(b) as allegedly being anticipated by Seiffert *et al.*, *The Journal of Biological Chemistry*, Vol. 275(44), pp. 34086—34091, (2000) ("Seiffert", hereinafter). Applicant respectfully traverses the rejection.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Applicant respectfully points out that Seiffert neither discloses each and every element of Applicant's claims as amended herein, nor describes Applicant's invention in complete detail.

The Examiner identifies one compound **1** on p. 34087 of Seiffert as allegedly anticipating Applicant's claims. It is a Boc-protected 3-amino caprolactam, with structure as follows:



Applicant thereby understands that the Examiner is interpreting compound **1** of Seiffert to correspond to Applicant's formulae (**I**) or (**I'**) where $X = -CO-R^1$ and R^1 is *t*-butoxy.

Applicant first notes that the Examiner states that the compound in Seiffert is for "treatment of Alzheimer's disease." Applicant finds no support for this statement in Seiffert. In fact, compound **1** is only referenced in Seiffert as a starting material for synthesis of various γ -secretase inhibitors. Therefore, Applicant does not believe that Seiffert provides evidence of a pharmaceutical application for compound **1** and, correspondingly, provides no disclosure of a pharmaceutical composition that contains **1**.

Furthermore, Applicant believes that the indiscriminate application of compound **1** to all of Applicant's claims is misplaced, for at least the following reasons.

Claims 1 and 2 are cancelled herein.

Claims 3 and 4 recite a pharmaceutical composition.

Claims 5 and 6 recite a genus of compounds from which the *t*-butyl alkoxy substituent has been deleted.

Claim 7 recites a pharmaceutical composition, and one in which the alkyl part of the R^1 radical is linear.

Claim 8 recites a pharmaceutical composition.

Claim 9 recites a pharmaceutical composition, and one in which the alkyl part of the R^1 radical contains 8 – 10 carbon atoms.

Claims 10 and 11 recites a pharmaceutical composition.

Claim 12 recites a pharmaceutical composition, and one in which the alpha-carbon of the R^1 substituent is chiral.

Claims 13 and 14 recite a pharmaceutical composition.

Claims 15, 16, 17 and 18 each recite a pharmaceutical composition comprising a compound selected from a list of compounds, none of which is identical to compound **1** of Seiffert.

Claims 19 and 20 recites a method of treatment using various pharmaceutical compositions, and therefore cannot be anticipated by the disclosure of compound **1** as a starting material in Seiffert.

Claims 21 and 22 recite a pharmaceutical composition.

Claim 23 recites a pharmaceutical composition, and one in which the R¹ substituent is not an alkyl group.

Claim 24 recites a pharmaceutical composition comprising a compound which is different from compound 1 of Seiffert.

Claim 25 recites list of intermediate compounds, none of which is compound **1** of Seiffert.

Claim 26 recites a pharmaceutical composition comprising a compound which is different from compound 1 of Seiffert.

Accordingly, Applicant respectfully submits that the disclosure of Seiffert does not anticipate Applicant's claims 3 – 26, and respectfully requests that the rejection be withdrawn.

By responding in the foregoing remarks only to particular positions taken by the examiner, Applicant does not acquiesce with other positions that have not been explicitly addressed. In addition, Applicant's selecting particular arguments for the patentability of a claim should not be understood as implying that no other reasons for the patentability of that claim exist. Finally, the Applicant's decision to amend or cancel any claim should not be understood as implying that the applicant agrees with any positions taken by the examiner with respect to that claim or other claims affected by such amendments.

CONCLUSION

In view of the above remarks, Applicant respectfully submits that the Application is in good and proper order for allowance. Withdrawal of the Examiner's rejections and early notification to this effect are earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the Application, the Examiner is encouraged to call the undersigned at (650) 419-2010.

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No fee is believed owed in connection with filing of this amendment and reply, other than the extension of time fees, and claim fees, separately authorized herewith.

Respectfully submitted,

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